Remarks

Claims 1-23 were pending. Applicants have canceled claims 1-7 and 12-23 without prejudice to Applicants' right to pursue their subject matter in the present application and in other applications. Applicants have amended claim 10 to recite that the fragment comprises at least 200 consecutive amino acid residues of SEQ ID NO:2, wherein the variant and said fragment have at least 90% sequence identity with each other. Support for the amendments to claim 10 is found in the original application at least, for example, in paragraphs **[0013]**, **[0043]**, **[0085]** and **[0117]** and in original claims 10 and 11. Support for the amendment to claim 11 is found in the original application at least, for example, in paragraphs **[0013]**, **[0043]**, **[0085]** and **[0117]**. Upon entry of the present amendment, claims 8-11 will be pending and presented for consideration.

Applicants have amended the title in view of the claim restriction. Applicants have amended the sequence listing to incorporate a sequence from FIG. 1; support for the amendment is found in FIG. 1 as originally filed. Applicants have amended the specification to incorporate additional sequence identifiers corresponding to the sequences presented in FIG. 1.

Applicants submit that the present amendment introduces no new matter into the application.

Objection to the specification

Applicants have amended the description of FIG. 1 in the specification to incorporate appropriate sequence identifiers and have amended the sequence listing to incorporate the sequence of SEQ ID NO: 304 from FIG. 1. Applicants submit that the application now fully complies with the sequence rules.

35 U.S.C. § 112, second paragraph

The Office action rejected claim 8 under 35 U.S.C. § 112, second paragraph, as allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which appliant regards as the invention" (Office action, p.3). Specifically, the Office action remarked

that "it is not clear what enzymic activity the said polypeptide is endowed with" (Office action, p.3).

Applicants request reconsideration and withdrawal of this rejection.

Applicants submit that the claim is in no way indefinite. The Office action itself correctly recognized that the claim is directed to an isolated polypeptide comprising a fragment of SEQ ID NO:2, wherein the fragment comprises at least 200 consecutive amino acids of SEQ ID NO:2. The claim is clear, definite, and unambiguous. The claim does not refer to any activity. The claim need not refer to any activity. The claim encompasses fragments of SEQ ID NO:2, whether they be, for example: immunogenically active (see, *e.g.*, paragraph **[0114]** of the application: "The present invention also contemplates immunogenic polypeptide fragments suitable for raising anti-CLPP1 antibodies"); active as a phosphatase (see, *e.g.*, paragraph **[0074]** of the application: "The phosphatase domain in CLPP1 can be used to dephosphorylate suitable substrates"); or inhibitory (see, *e.g.*, paragraph **[0114]** of the application: "isolated CLPP1 polypeptides and mutated CLPP1 polypeptides capable of inhibiting normal CLPP1 activity").

The scope of the claim is clear. "If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph" (M.P.E.P. § 2173.04).

Applicants request reconsideration and withdrawal of the rejection.

The Office action also rejected claim 10 under 35 U.S.C. § 112, second paragraph, alleging that the phrase "fragment includes" was unclear, but suggesting that "fragment comprises" would be clear. Without acquiescing to the rejection, Applicants have replaced "fragment includes" in claim 10 with "fragment comprises." Applicants therefore request reconsideration and withdrawal of the rejection.

The Office action also rejected claim 11 under 35 U.S.C. § 112, second paragraph, alleging that it was unclear whether the recited sequence identity was intended to refer to identity

between the variant and the fragment as compared to each other or to identity between the variant and fragment as compared to SEQ ID NO:2. Applicants disagree with the rejection, but have amended claim 11 to recite that the variant and said fragment have at least 95% sequence identity with each other. Applicants therefore request reconsideration and withdrawal of the rejection.

35 U.S.C. § 112, first paragraph

The Office action rejected claims 8-11 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. According to the Office action, "[c]laims 8-11 are rejected under this section 35 U.S.C. 112 because the claims are directed to a 'genus' of polypeptides without any associated function" (Office action, page 4). The Office action argued that the information in the application "is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus of polypeptides" and that "[t]herefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention" (Office action, page 5).

Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 8-11 do indeed define a genus of polypeptides and do so strictly by reference to physical characteristics of the polypeptides. Claim 8, for example, relates to an isolated polypeptide comprising a fragment of SEQ ID NO:2, wherein said fragment comprises at least 200 consecutive amino acid residues of SEQ ID NO:2. Thus, the subject matter of claim 8 is defined by the sequence of SEQ ID NO:2 and its fragments of at least 200 consecutive amino acids. One of skill in the art at the time the application was filed, upon reviewing the application, could have immediately envisioned the entire "genus" of fragments of at least 200 consecutive amino acids and would have recognized any polypeptide comprising such a fragment. According to the Manual of Patent Examining Procedure, "Possession may also be shown by a clear depiction of the invention . . . in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed

invention." M.P.E.P. § 2163(II)(A)(3)(a). Here, the fragments of SEQ ID NO:2 are indeed described formulaically, such that possession of the entire genus is evident. Nothing in 35 U.S.C. § 112 requires an applicant to claim an invention in terms of its function. Indeed, the written description guidelines and the Manual of Patent Examining Procedure favor structural descriptions over functional ones.

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide relevant evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure . . . .
>
> For some biomolecules, examples of identifying characteristics include a sequence, structure . . . .
>
> Although structural formulas provide a convenient method of demonstrating possession of specific molecules . . . .
>
> A definition by function alone does not suffice to sufficiently describe a coding sequence because it is only an indication of what the gene does, rather than what it is.
>
> M.P.E.P. § 2163(II)(A)(3)(a) (internal quotations omitted)

Thus, claim 8 comports fully with the written description requirement of 35 U.S.C. § 112. Similarly, claims 9-11 define inventions structurally by reference to variants or fragments of SEQ ID NO:2, wherein the variants and fragments have at least 90% or at least 95% sequence identity with each other. Because these claims are defined structurally, such that one of skill in the art would have recognized the members of the genus at the time the application was filed, claims 9-11, like claim 8, comport fully with the written description requirement of 35 U.S.C. § 112.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

The Office action also rejected claims 8-11 under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for a polypeptide with SEQ ID NO:2 having calcineurin-like phosphoesterase activity," allegedly does not enable practice of the invention commensurate in scope with the claims. According to the Office action: "The specification is

limited to teaching the making and using of SEQ ID NO: 2 as [a] calcineurin-like phosphoesterase, but provides no guidance with regard to the making of variants and mutants or with regard to other uses."

The Office action is mistaken.

"With regard to other uses"

As but one example, the application teaches the use of variants or fragments of CLPP1 to immunize a vertebrate for antibody production (application, paragraph **[0133]**). "Immunogenic fragments (epitopes) of CLPP1 can be identified using well known techniques. In general, any fragment of SEQ ID NO:2 can be used to raise antibodies specific to CLPP1." Application, paragraph **[0134]**. Pages 35-39 of the application detail various methods by which these fragments or variants can be used to generate antibodies to CLPP1 and uses of such antibodies. Applicants submit that it was well within the level of skill in the art to use, as immunogens, polypeptides comprising fragments of SEQ ID NO:2, wherein said fragment comprises at least 200 consecutive amino acid residues of SEQ ID NO:2. Similarly, it was well within the level of skill in the art to use a variant of such a fragment as an immunogen (*e.g.* to enhance an immune response, or to improve solubility, or to facilitate protein preparation, *etc.*).

The application fully enables the use of polypeptides comprising fragments of SEQ ID NO:2 or variants thereof, wherein the variant and said fragment have at least 90% sequence identity with each other. One of skill in the art could practice the invention without undue experimentation. Accordingly, the application enables the practice of the invention in a manner commensurate in scope with the claims and the rejection should be reconsidered and withdrawn.

"Guidance with regard to the making of variants and mutants"

The application discloses that amino acid residues 47 to 211 of CLPP1 are 91.3% identical to the consensus sequence of the calcineurin-like phosphoesterase family (see, for example, application paragraph **[0231]**) and that similar portions of CLPP1 have significant homologies to other phosphatases (see application paragraph **[0230]**). Thus, the application does provide guidance with regard to the making of variants and mutants that retain enzymatic activity. For example, the application suggests to one of ordinary skill in the art seeking to make

a fragment of SEQ ID NO:2 having enzymatic activity that it may be advantageous to include some or all of the region around residues 47-211. Similarly, FIG. 1 of the application provides an alignment of the consensus sequence of the calcineurin-like phosphoesterase family with the relevant residues of SEQ ID NO:2. By identifying the amino acids that are not conserved, the application announces to one of ordinary skill in the art the identity of amino acid residues that are more likely to be changeable without destroying enzymatic activity, and suggests amino acids to which those residues could be changed. As acknowledged by the Office action, "enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims." When, as here, the application provides guidance regarding what types of fragments or variants may be useful, screening such fragments and variants for a desired activity is routine and not undue.

Accordingly, in view of the specific, relevant guidance provided by the application and the usefulness of the claimed polypeptides regardless of enzymatic activity, the application enables the practice of the invention in a manner commensurate in scope with the claims. Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

Upon entry of the present amendment, claims 8-11 will be pending and presented for consideration. Applicants believe the claims to be in condition for allowance and request a telephonic interview with the undersigned attorney to address any outstanding issues.

Respectfully submitted,

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